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Supplementary Material for Lewis et al 2017

Figure S1. Flow chart of patients

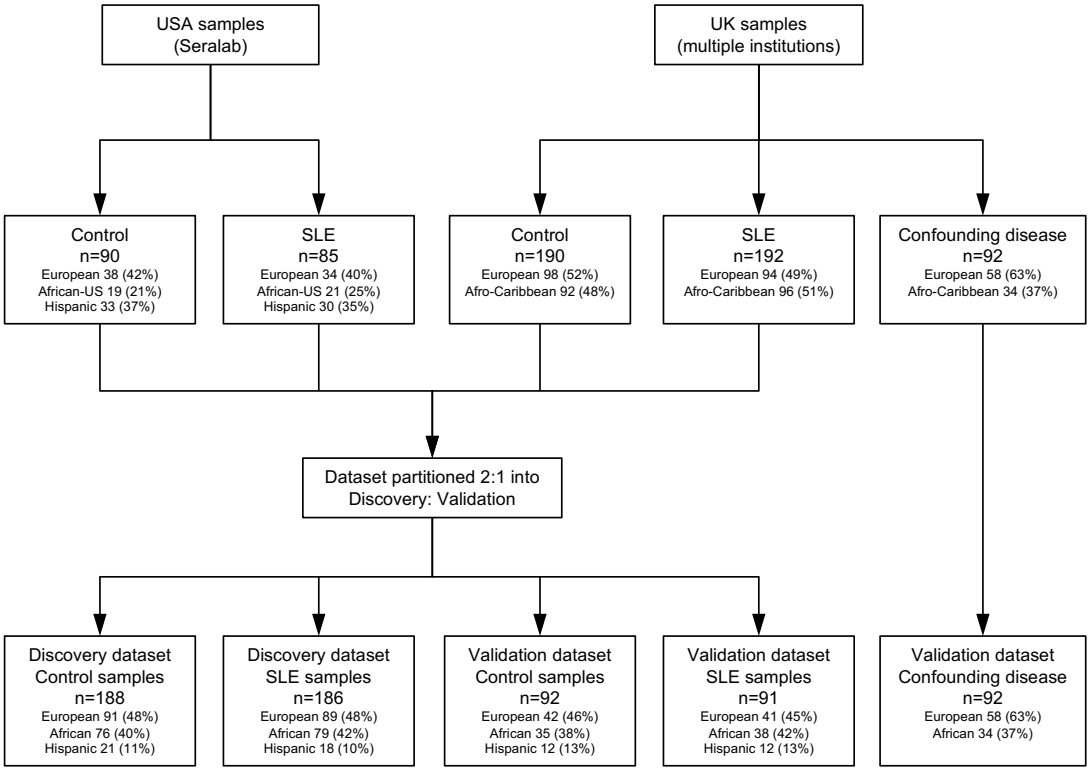


Figure S2. Principal component analysis of discovery and validation datasets

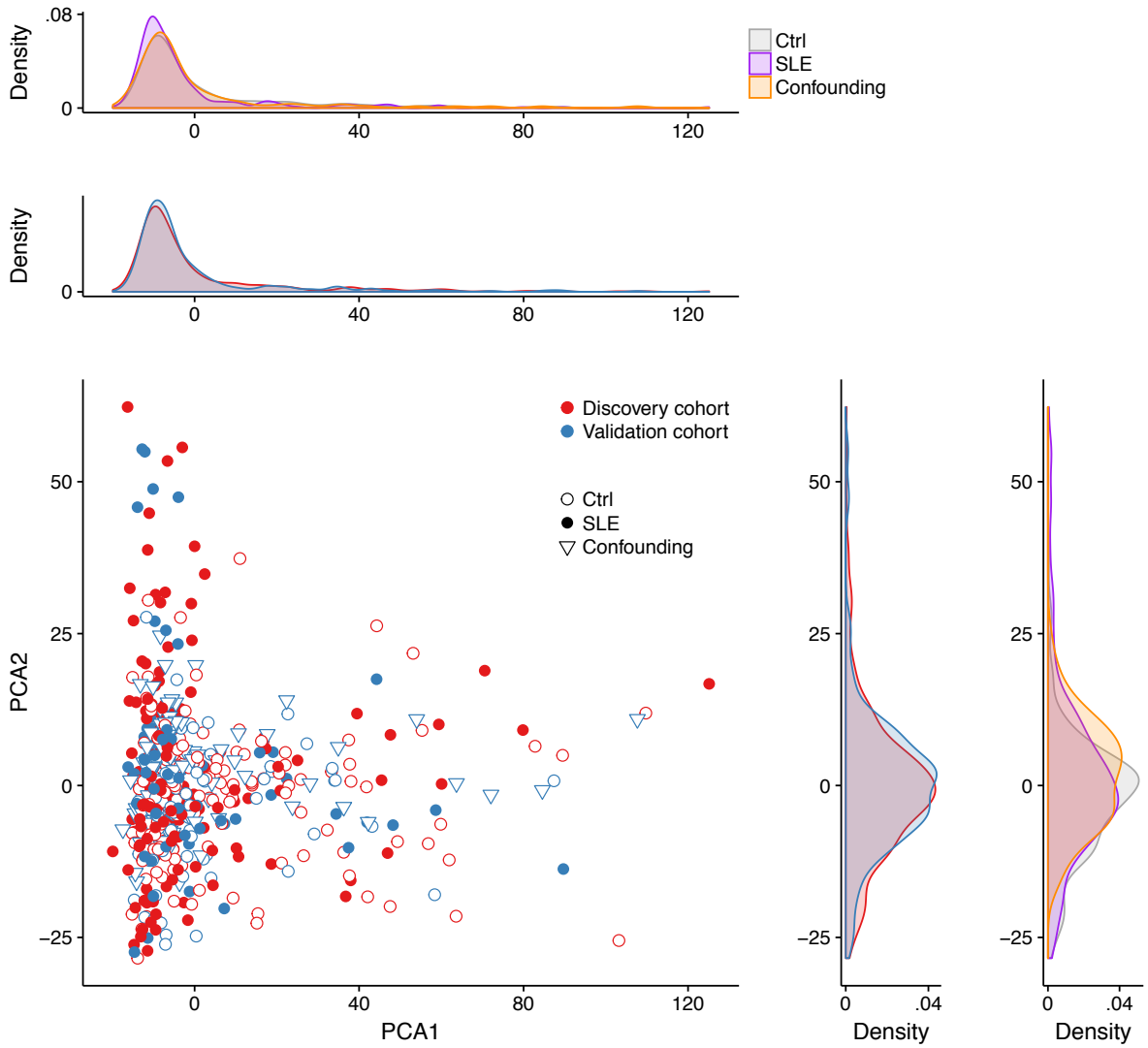


Figure S3. Reduced subspace heatmap showing differences between in autoantibody levels across four SLE subgroups in discovery and validation datasets

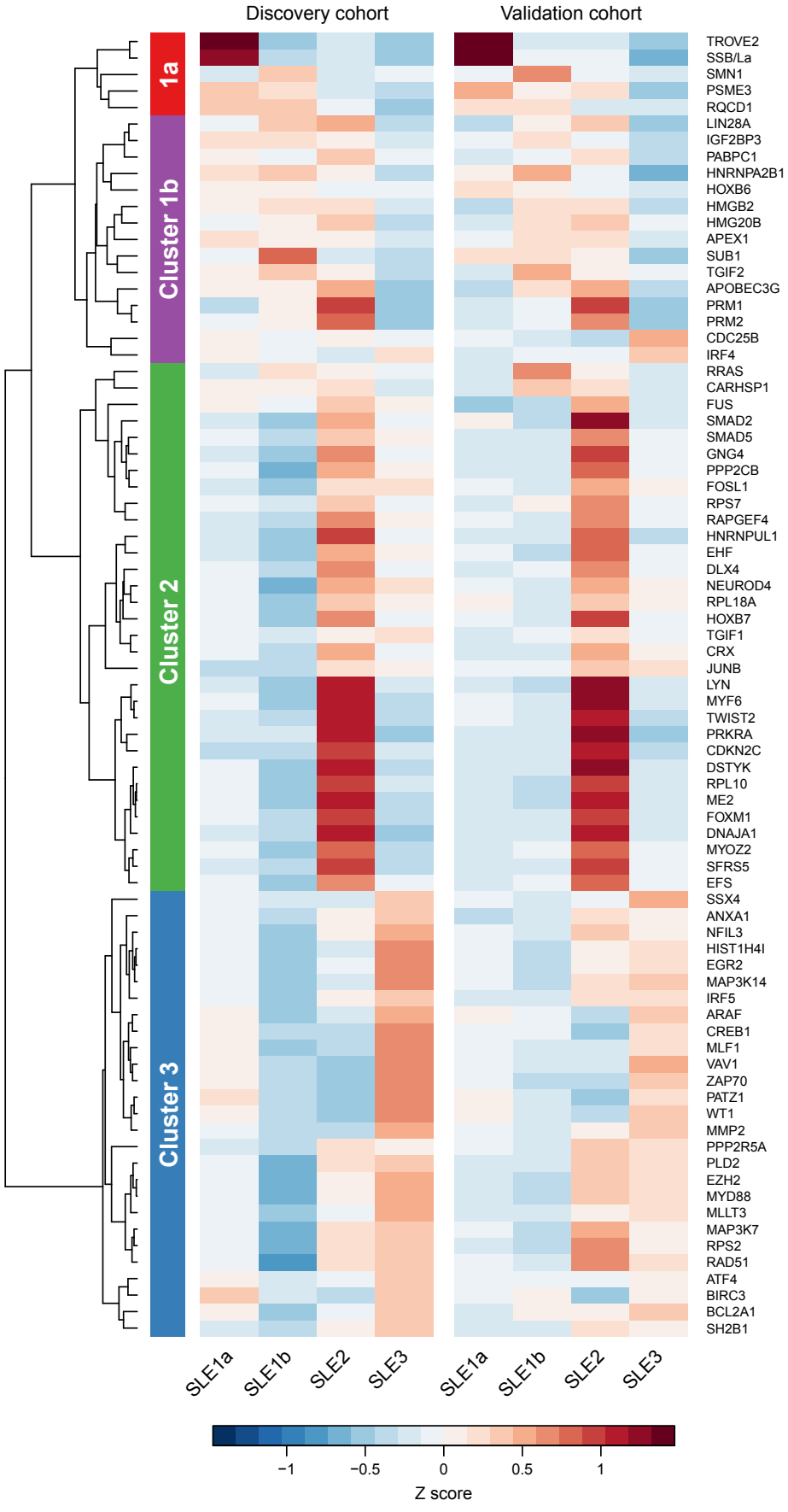


Figure S4. Principal component analysis of autoantibody levels in SLE individuals and controls

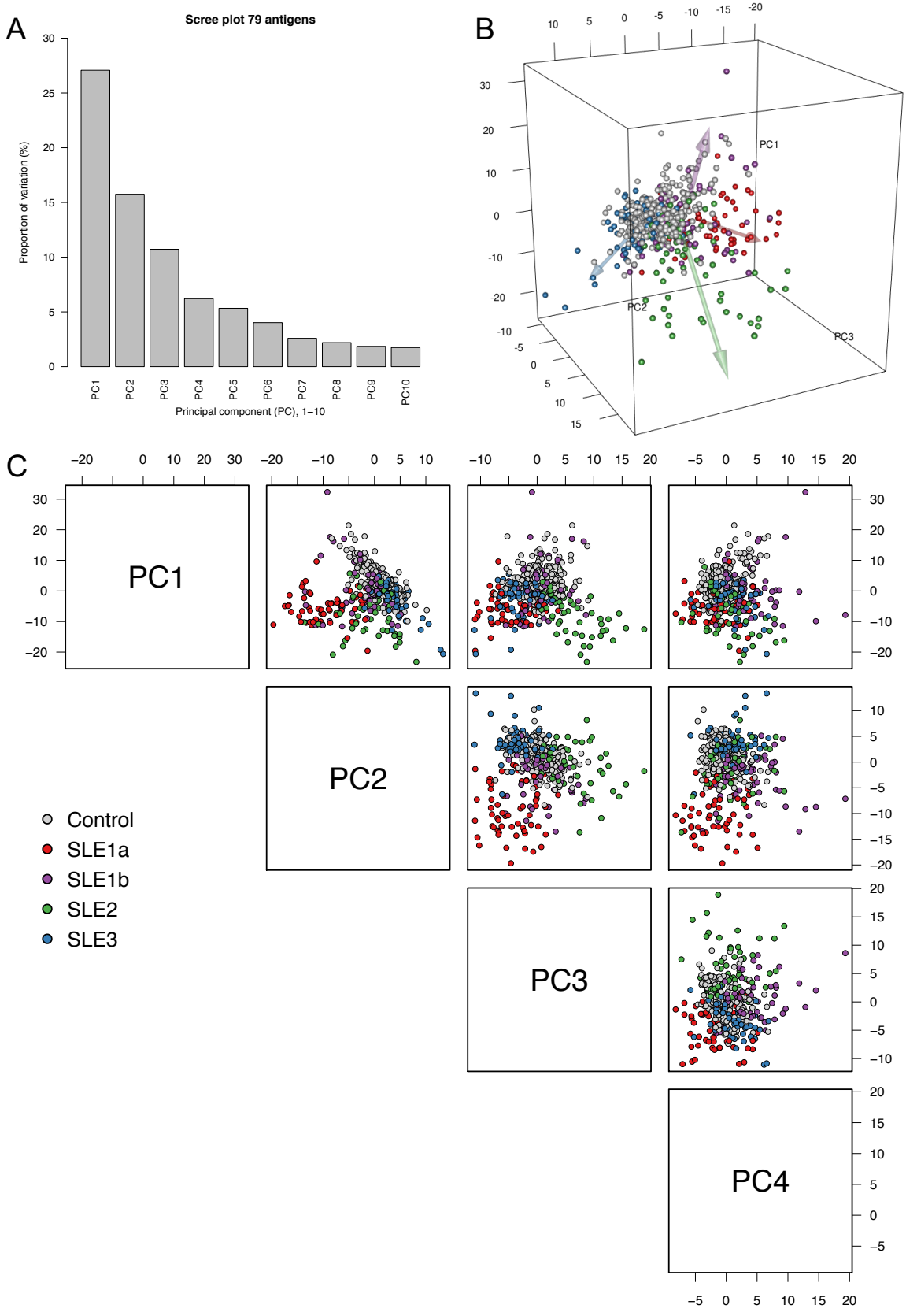


Figure S4

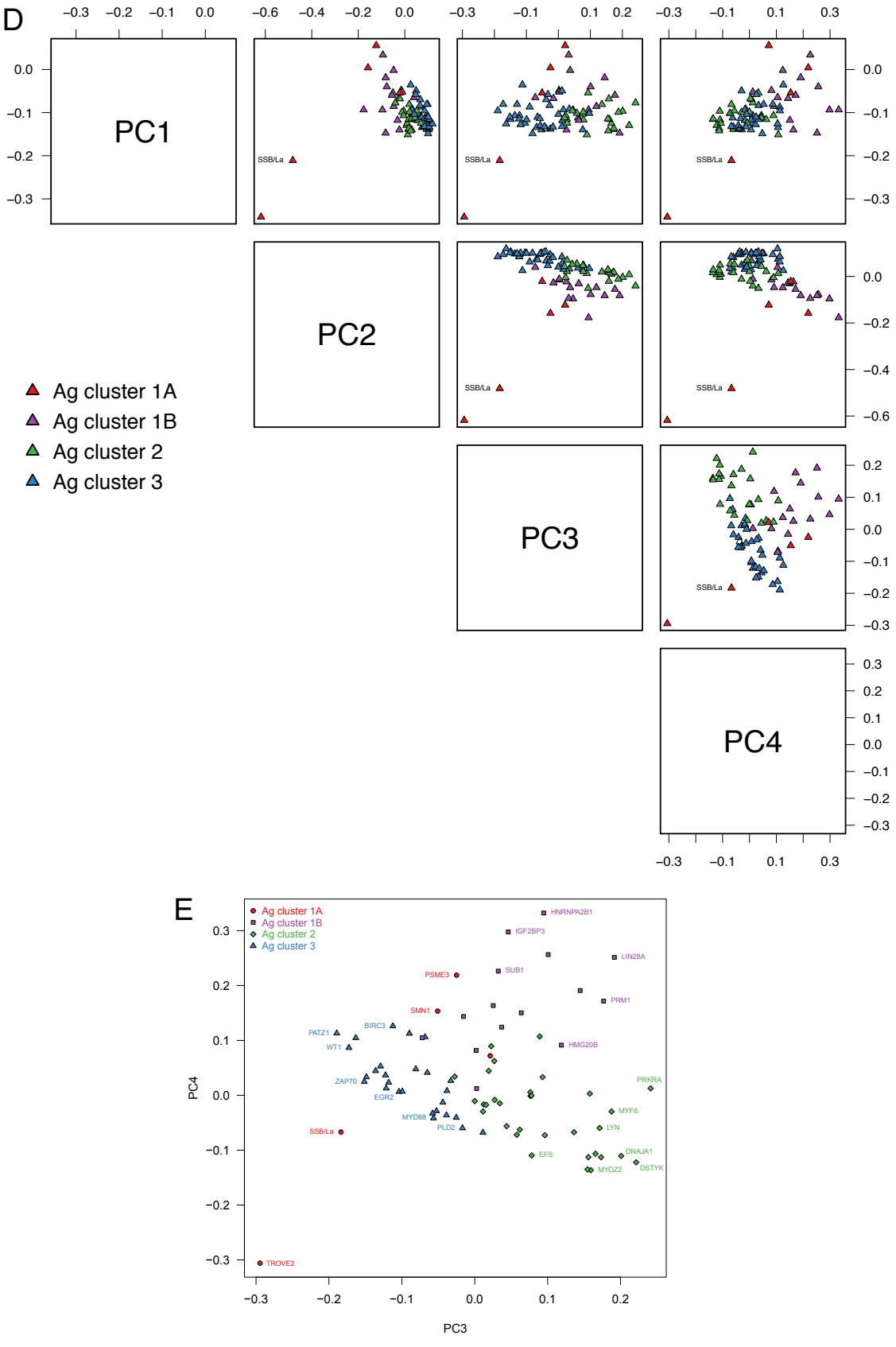

D
PC1
PC2
PC3
PC4
SSB/La
Ag cluster 1A
Ag cluster 1B
Ag cluster 2
Ag cluster 3
E
PC4
PC3
HNRNPA2B1
IGF2BP3
LIN28A
PSME3
SUB1
PRM1
SMN1
BIRC3
PATZ1
WT1
HMG20B
ZAP70
EGR2
PRKRA
MYD88
PLD2
MYF6
LYN
EFS
DNAJA1
MYOZ2
DSTYK
TROVE2

Figure S5. Distribution of autoantibody positivity by ancestry
Stacked barchart showing distribution of ancestry across SLE patients for each autoantibody. P value calculated by Fisher exact test, with FDR correction.

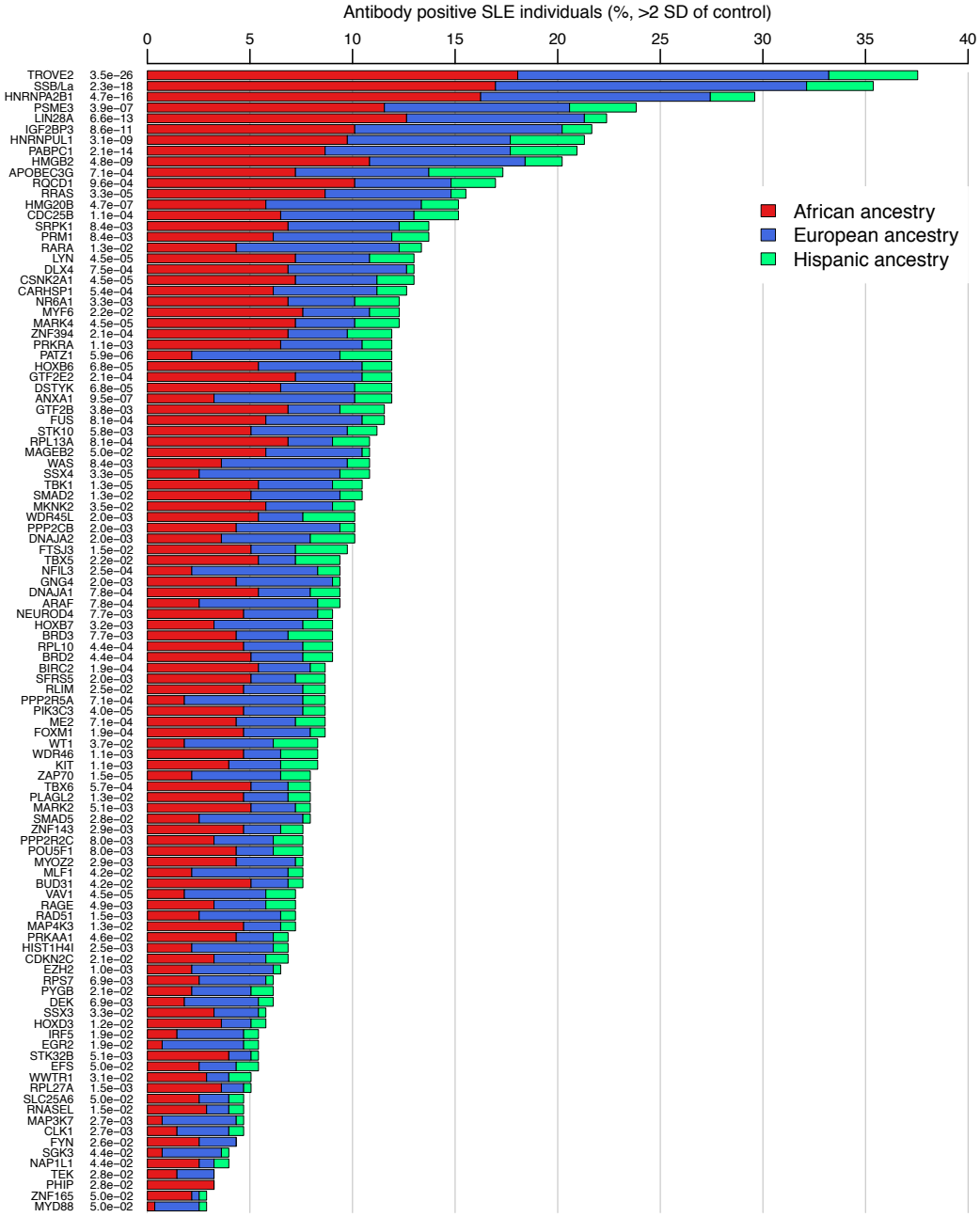
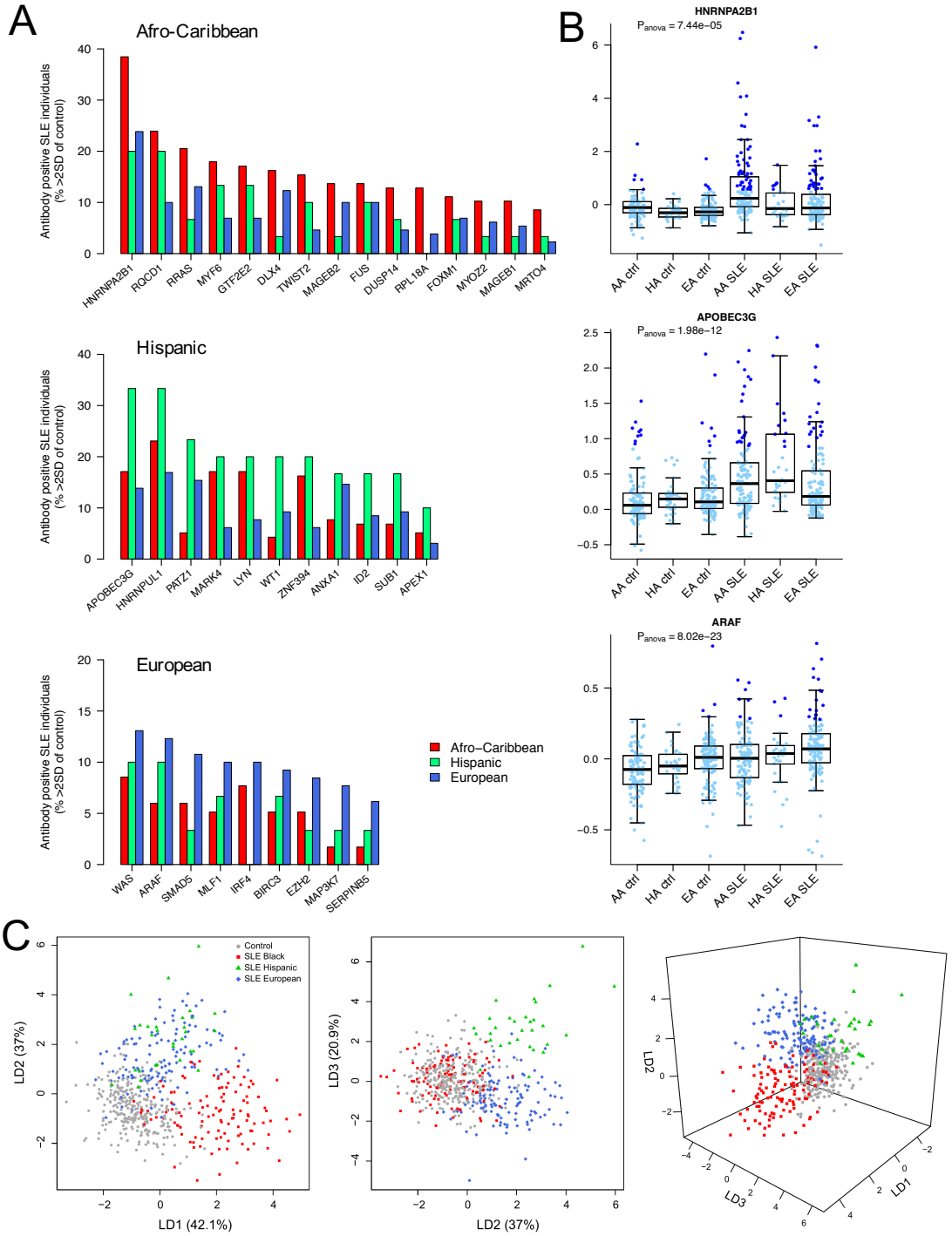


Figure S6. Distinctive SLE autoantibodies profiles according to ancestry

(A) Differential antibody positivity according to ancestry, showing autoantibodies with increased positivity in Afro-Caribbean (AA) SLE, Hispanic (HA) SLE and European (EA) ancestry SLE. Autoantibodies were selected as statistically different between SLE ancestral groups by one-way ANOVA (FDR corrected P<0.01). (B) Boxplots of key autoantigens specific for different ancestries in SLE. (C) Linear discriminant analysis based on plots showing separation of Afro-Caribbean, Hispanic and European ancestry SLE individuals according to linear discriminant factors LD1, LD2 and LD3. Right hand panel, 3-dimensional plot of LD1, LD2 and LD3. (D) Table of LDA predicted categorisation of SLE ancestral groups and control individuals compared to observed groupings.



		Predicted		
	Control	SLE AA	SLE HA	SLE EA
Observed				
Control	**262**	8	0	10
SLE AA	22	**89**	1	5
SLE HA	5	0	**24**	1
SLE EA	33	4	4	**89**
Misclassified	16.7%			

Figure S7. Effect of HLA alleles on autoantibody levels in SLE
Autoantigens colour-coded by cluster (red=1a, purple=1b, green=2, blue=3). P values (without adjustment for multiple testing) were calculated by fitting a linear regression model including antibody titre and genetic population structure PC1-4. Dark blue dots represent antibody positivity defined as >2 SD of control population.

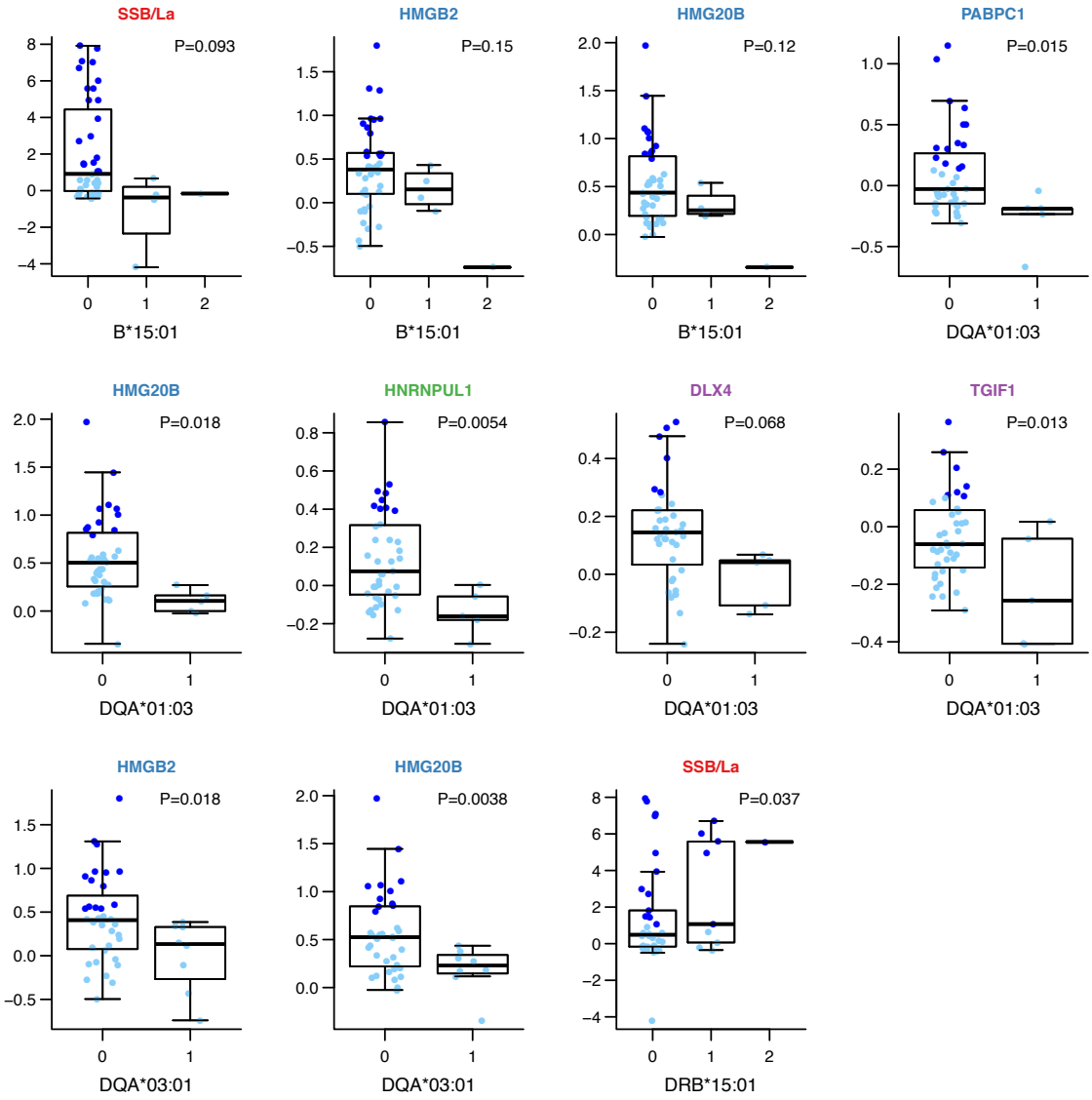


Figure S8. Cross-validation of elastic net binomial regression model
10-fold cross-validation was performed on the discovery dataset to tune L1-L2 penalisation parameter α and shrinkage parameter λ by minimising binomial deviation.

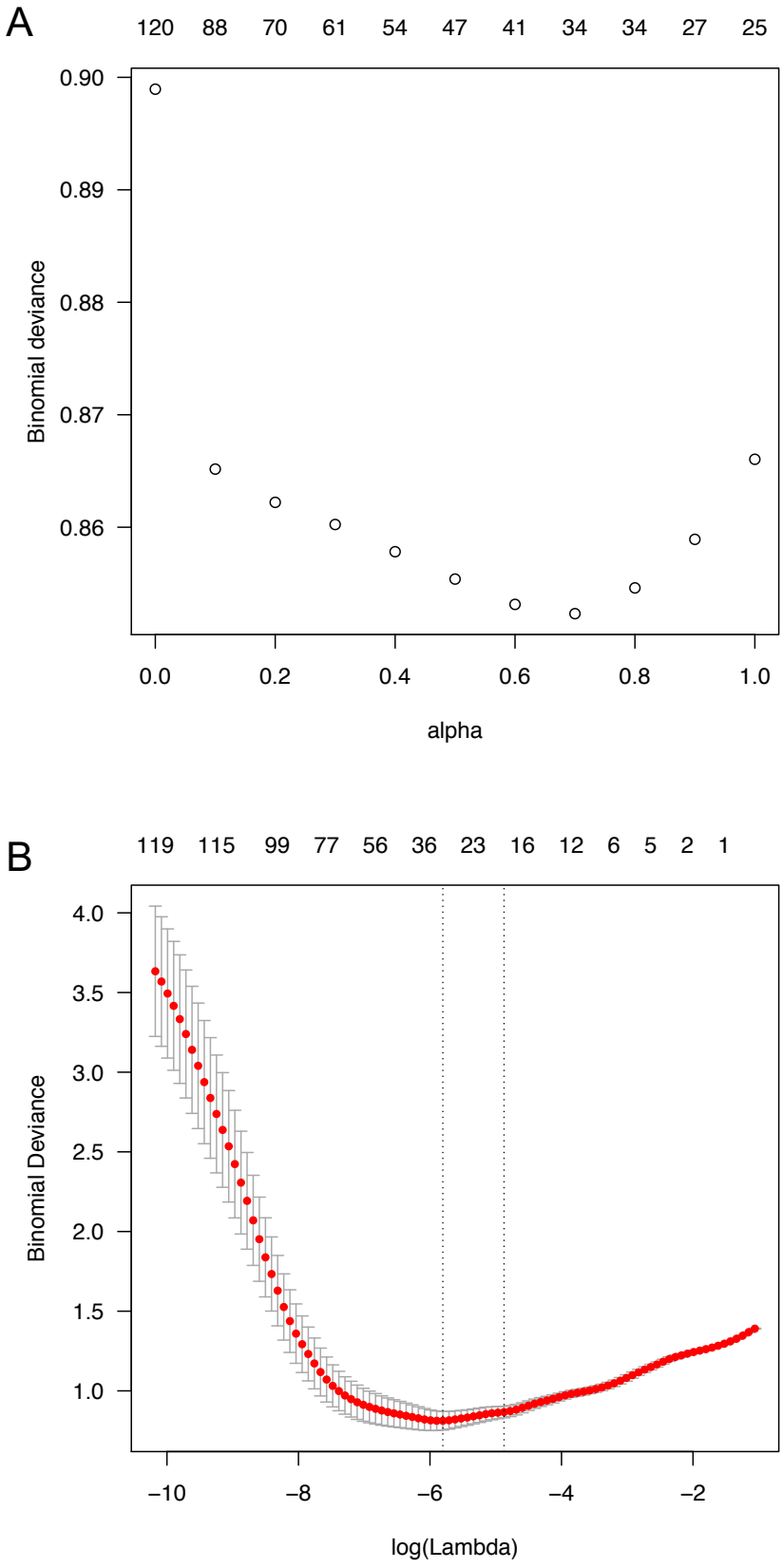


Figure S9. SLE cluster heatmap of binomial regression model autoantibodies

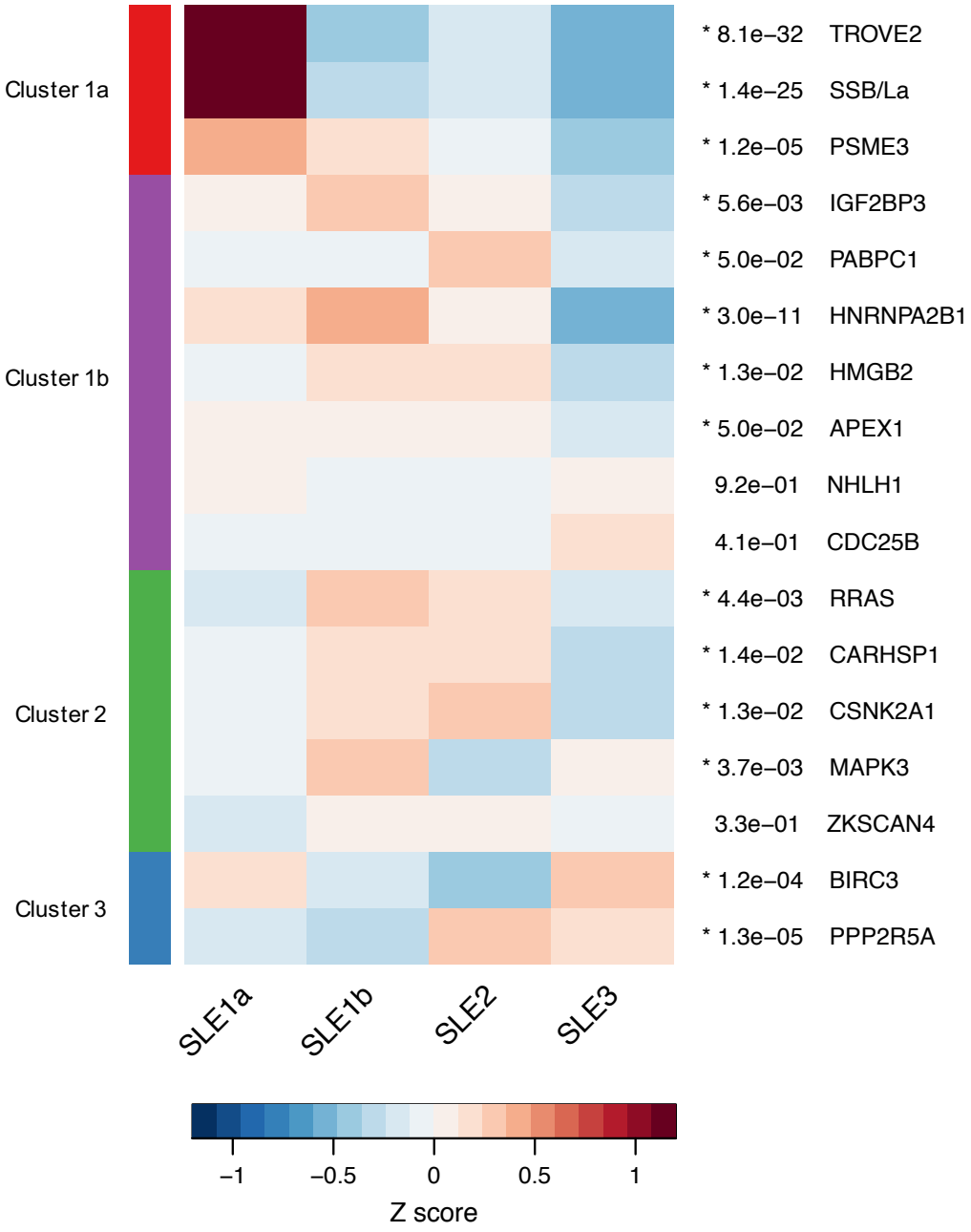


Figure S10. ROC curve analysis of mixture discriminant analysis model incorporating ANA and dsDNA antibodies

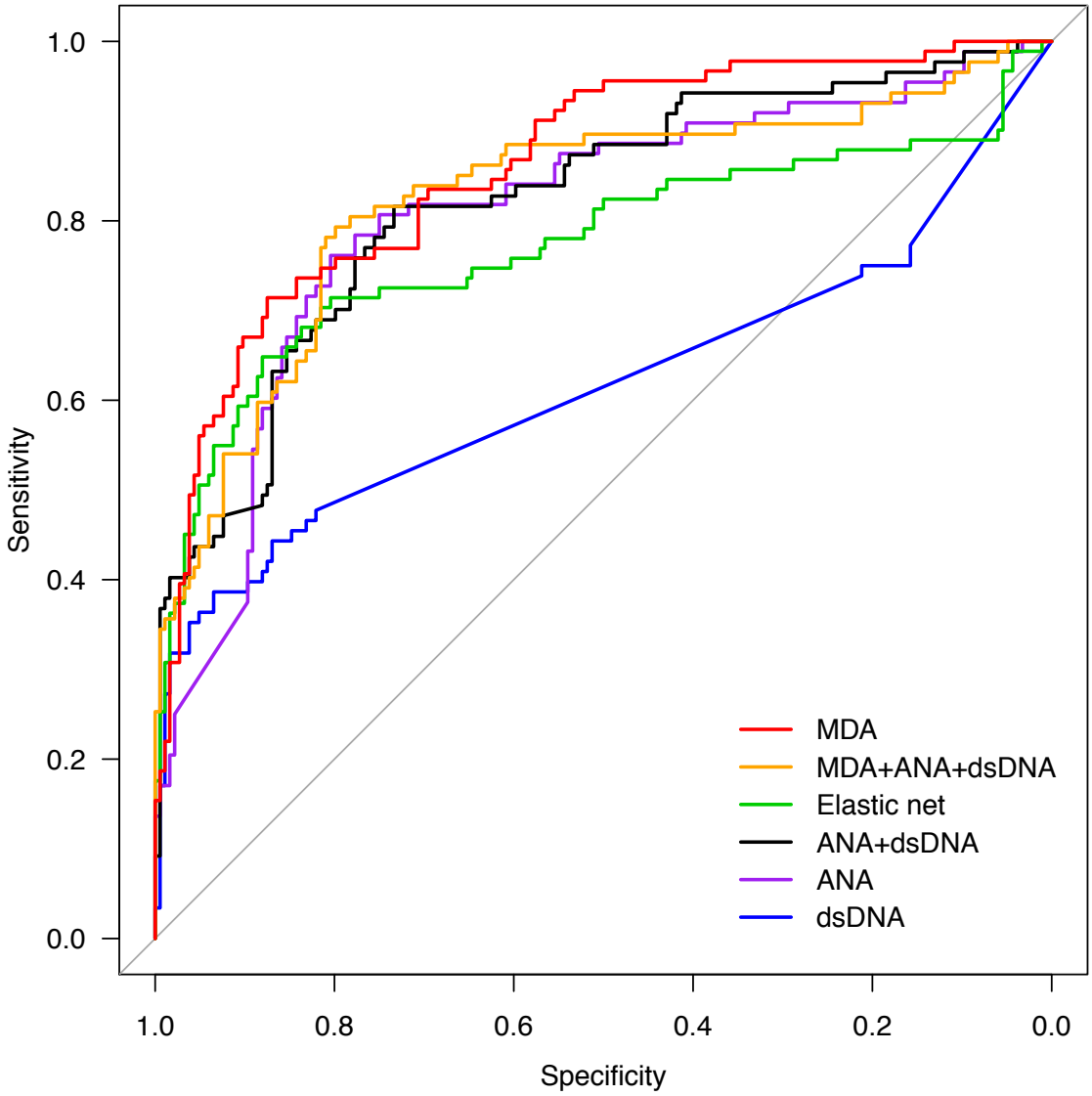


Figure S11. Canonical variate plot of mixture discriminant analysis model
Canonical variate plots from 26-autoantibody mixture discriminant analysis (MDA) model showing 4 SLE clusters and 1 control cluster in (A) discovery and (B) validation datasets. Cluster centroids are marked C for 1 control centroid and S for 4 SLE centroids.

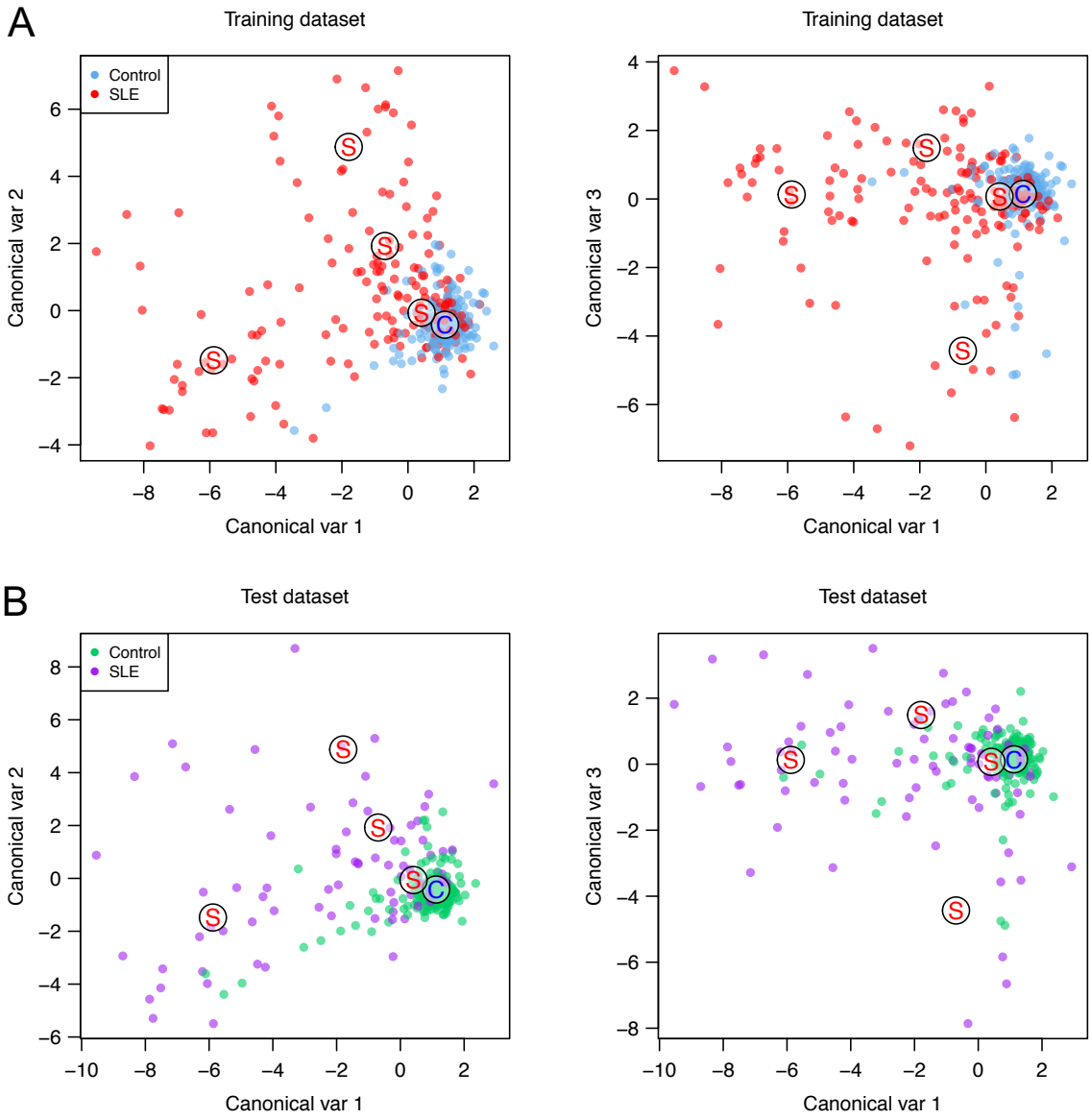


Figure S12. Heatmap of autoantibody levels grouped by ancestry for 26-autoantibody multinomial regression model